CHAPTER VI: COMPLEMENTARY AND ALTERNATIVE MEDICINE AND AGING

Men's Aging Issues

Now let me turn to men. Not to be completely ignored. The question is, is there a role for CAM, or complementary and alternative medicine, interventions in treating either benign enlargement of the prostate, which is virtually a hallmark of aging in men— if you live long enough, it's going to happen— or malignant disease of the prostate, namely prostate cancer, which is, as I've already said, even more common. One out of 6 newborn boys will develop prostate cancer. One out of 8 newborn girls will develop breast cancer unless we can think of some clever way to prevent that from happening.

So let's start with benign disease because it's, thankfully, more common than malignant disease. In 1989, and the numbers, of course, are escalating enormously because of the graying of the population, but in 1989, 1.3 million physician office visits were for this purpose. And 170,000 men underwent removal of some or all of their prostates. About ¼ of the men who were Caucasian, because there are differences in African-American men and other populations, who were age 50 to 79, met standardized criteria for discussing options about having treatment for this enlargement. The burden, that is, the number of men who are affected, as you can easily imagine, far exceeds the number of men who are being evaluated and treated properly, which is a better way of saying that utilization is less than burden. The implications for morbidity and mortality even independent of prostate cancer, which we'll get to, are enormous.

There are specialists in treating men with this particular problem. The classic treatment is some form of surgery, which has been made progressively more sophisticated with newer techniques. To the dismay of the urological and surgical community, there has been a medicalization of this problem by new and clever mainstream medicines—the most well known being Proscar, which basically is an enzyme inhibitor of the prostate that prevents male hormone from stimulating growth of the prostate, and it does it very effectively.

Then there are other medicines. But what we're here to talk about is not that. We're here to talk about alternative or complementary and alternative medicines or phytotherapy or plant therapy. So let's turn to that.

So this is a list of various plant extracts commonly used in this and other countries to treat lower urinary tract symptoms, both the irritative and obstructive kind, in men with benign prostatic hyperplasia, or BPH. They include saw palmetto, the best of them, which is posing for the camera here, in a field in Florida. There have been a number of studies. In this and the next slide is simply a summary, what we call a meta-analysis, sort of a review and critique of 18 particular studies, and this critique was published a few years ago about efficacy and safety. The bottom line is that this analysis of 18 different, small-scale but well-done, carefully controlled studies in men with BPH on saw palmetto showed improvement in obstructive urinary symptoms in a substantial number, as you can see, anywhere from sort of 1/4 to 40% on the average. When it was compared with Proscar, which goes by the generic name finasteride, or placebo, it was safe, and in fact, was less likely to cause erectile dysfunction or impotence than was the mainstream medicine, which does that, not surprisingly, because one of it's mechanisms of action is to cut down on the effects of male hormone. So that suggested that this might be a useful thing to use. But all the data were in small-scale studies. So again, oftentimes to answer 1 or 2 important questions—is it effective in doing this and is it safe—you need to have large-scale or multicenter studies. So NCCAM, in partnership with the Office of Dietary Supplements, ODS, and one of the other NIH institutes, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), is conducting a several-year study in 3,000 men to compare saw palmetto and another CAM agent, and placebo using standardized criteria. We'll have the answer in a few years as to whether this is really a safe, effective, and reasonable thing to do as suggested by these smaller studies.

Now I want to talk about a more malicious, as we conclude, a more malicious problem, namely prostate cancer. Firstly, prostate cancer is increasing. Why is it? Is it really increasing or is the detection increasing? Most of us believe it's a combination of both, but detection has clearly increased with the advent of the blood test for your prostate,

namely the prostate-specific antigen blood test, or the PSA. It's very clear that the use of this blood test, which began more or less when you see that outtake in both of these curves, has led to increasing detection. Just as mammography and the advent of it led to an increased detection of breast cancer before there was mammography. You will also notice a difference between Caucasian men and African-American men. African-American men had a substantially higher incidence and prevalence, that is, they have more prostate cancer. The death rates of the most common cancers, and if you look at the prostate, you'll notice the death rate, unlike the incidence rate, hasn't really changed a whole lot. There's a little bit of an uptake, but not really. So it's detection that's really the big deal. Much of it is more scrutiny, both with the blood test and just more awareness among men that this is something they have to pay attention to as they get older, and more attention among health care providers that this is something they have to look for as men get older.

I've already mentioned that there's a difference between Caucasian men and African-American men— there is, as you can see, in virtually every age group from 50 and up. African-American men have substantially more prostate cancer, and we're just beginning to understand some of the genetic and nongenetic reasons why that might be the case.

There are a variety of CAM approaches to treating prostate cancer. Let me focus on these for a moment by saying that they all relate to some of the general nonprostate manifestations that occur in men with prostate cancer either before or after they are treated because, again, the bad news is so many men have this. The bad news is that so many men die of this, as women do with breast cancer, but the good news is our treatments for both of these conditions are better, and people are living longer, both men in the case of prostate and women in the case of breast. But one of the things that carries with this added longevity in both sexes, and right now we're talking about men, is they develop a lot of the aggregate side effects of having been made testosterone deficient— just as women would accumulate a lot of the side effects of becoming estrogen deficient. We're now trying to pay attention to some of those by better medical management. But one of the CAM interventions that had received a tremendous amount of visibility and

press was a particular agent called PC-SPES, which is no longer available, and I'll tell you why. Firstly, PC-SPES was classified as a dietary supplement of Chinese background with 8 different botanicals in it. It was used for men with advanced prostate cancer. And in this country alone, it is estimated that approximately 30,000 men, give or take, until recently, and perhaps even today, were using PC-SPES in addition to their mainstream interventions that were part of the treatment of their advanced prostate cancer. Small studies suggested that this was a safe substance, that it improved the quality of life, that it reduced pain, for example, bone pain, and lowered levels dramatically of this prostate cancer enlarger, PSA. In fact, this prestigious journal, the *New England Journal of Medicine*, just a few years ago published a paper that, in addition to doing these positive things, it had some kind of negative effects in that it had some effects on the female hormones, like estrogen. It's actually known that making a man less male-hormone-like, which by definition would make him relatively more female-hormone-like, is part of the treatment, classically, of patients with prostate cancer. Whether it be removal of the testes, which was an old form of treatment, to the more contemporary treatment where this is done medically with agents that can turn on and off, like a rheostat, male hormones for therapeutic benefit. But what happened along the way? Because this sounds awfully good. What happened along the way was something not good. There was one company in the U.S. in Southern California that was licensed to procure and make and package this hormone, obtaining it from a source in China where these herbs are derived from. The bottom line was about 15 months or 1½ years ago, the major state testing laboratory in California and the Department of Health evaluated the product, and they found that not only was it contaminated with things that shouldn't be there, but much more importantly, it was probably adulterated with things that absolutely are not natural and shouldn't be there. What kinds of things you might ask? Well, diethylstilbestrol, which is a manmade, artificial estrogen, which is very powerful, and used to be, 30 years ago, a form of treatment for men with prostate cancer, which we've since abandoned because it has too many adverse effects on heart function; Coumadin, a blood thinner, which can occur in natural forms in foods or in substances like it, but the way it was found was something that's manmade, not naturally occurring; indomethacin, or Indocin, which many of you may use for arthritis, which is not a naturally occurring substance. It's made in a

pharmaceutical house. So somewhere along the line, nefarious deeds were done. What did this do? It led to a serious problem. The U.S. Food and Drug Administration removed this from the market as it said on the previous slide. Those of us who care, which is everyone in this room and beyond this room, were dismayed, not only by the duplicity involved, but how are we going to deal with those 30,000 men who have advanced prostate cancer who believe they're getting some benefit or will get some benefit from this agent. I'll leave you that as an open-ended question with which many of us are wrestling at the moment.

So there's another trial that's really a biggie. Selenium and vitamin E are 2 substances; we've already seen that there's a difference between Caucasians and African-Americans in prostate cancer and death related to it. I'm not going to talk about this particular trial. I'm going to focus on this. A variety of laboratory studies and population studies, or epidemiological studies, which really means population studies, and some smaller-scale studies that were interventionist, suggest that selenium and vitamin E might prevent the development or progression of prostate cancer. So that led to what is now the largest study in the U.S. ever of attempt to chemo-prevent a cancer. The study is called the SELECT study. What is that study? It's a study to try to prevent the new development of prostate cancer. That's the primary endpoint—prevention. Other outcomes include: overall survival; cancer-free survival; heart, that is, cardiovascular events; and QOL, that is to say quality of life—these are all secondary measures in this study. The intervention is selenium, which you can buy over-the-counter, and vitamin E, or alpha-tocopherol. Nearly 36,000 men are going to be in this study led by the National Cancer Institute, NCCAM, and some others. Caucasian men will be 55 years or older upon entry, but because of the much higher frequency and earlier frequency and all the things I've shown about the difference in African-American men, the African-American men at entry will be a little younger for the reasons that are obvious here. These men will be followed for a long period of time at 6-month intervals. DRE refers to a digital exam, that is the doctor examining the patient's prostate manually, and a blood test, prostate function. This is an enormous study, as you can immediately imagine, that will help tell us whether this is

really a useful preventative measure as contrasted with a treatment measure. If it is, it will be exciting indeed.

To conclude with regard to men, this gentleman is someone who is probably very familiar to all of you. As you can see, George Burns was in that most radically growing age demographic group, the centenarians, with Gracie, of course. I guess for those of you who are psychologically inclined, and endocrinologically inclined, you might also say that sometimes a cigar is just a cigar.